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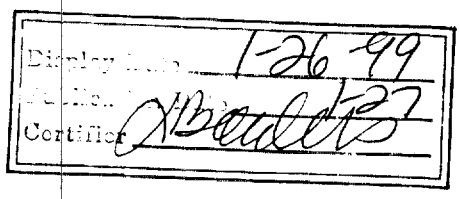
DEPARTMENT OF HEALTH AND HUMAN SERVICES




Food and Drug Administration

[Docket No. 98N–0721]

## Agency Information Collection Activities; Submission for OMB Review; Comment Request; Premarket Approval of Medical Devices

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing that the proposed collection of information listed below has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995 (the PRA).

**DATES:** Submit written comments on the collection of information by (*insert date 30 days after date of publication in the* **Federal Register**).

**ADDRESSES:** Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

**FOR FURTHER INFORMATION CONTACT:** Peggy Schlosburg, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1223.

**SUPPLEMENTARY INFORMATION:** In compliance with section 3507 of the PRA (44 U.S.C. 3507), FDA has submitted the following proposed collection of information to OMB for review and clearance. In the **Federal Register** of October 6, 1998 (63 FR 53675), the agency requested comments on the proposed collection of information. No comments were received.

Due to a clerical error, the title of the information collection that appeared in the **Federal Register** of October 6, 1998, was incorrect. The correct title follows.



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**I. Premarket Approval of Medical Devices—21 CFR Part 814 and FDAMA Sections 201, 202, 205, 207, 208, 209 (OMB Control Number 0910–0231—Extension)**

Section 515 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360e) sets forth requirements for premarket approval of certain medical devices. Under section 515 of the act, an application must contain several pieces of information, including: Full reports of all information concerning investigations showing whether the device is safe and effective; a statement of components; a full description of the methods used in, and the facilities and controls used for, the manufacture and processing of the device; and labeling specimens. The implementing regulations, contained in part 814 (21 CFR part 814), further specify the contents of a premarket approval application (PMA) for a medical device and the criteria FDA will employ in approving, denying, or withdrawing approval of a PMA. The purpose of these regulations is to establish an efficient and thorough procedure for FDA's review of PMA's for class III (premarket approval) medical devices. The regulations will facilitate the approval of PMA's for devices that have been shown to be safe and effective and otherwise meet the statutory criteria for approval. The regulations will also ensure the disapproval of PMA's for devices that have not been shown to be safe and effective and that do not otherwise meet the statutory criteria for approval.

Under § 814.15, an applicant may submit in support of a PMA studies from research conducted outside the United States, but an applicant must explain in detail any differences between standards used in a study to support the PMA's and those standards found in the Declaration of Helsinki. Section 814.20 provides a list of information required in the PMA, including: A summary of information in the application, a complete description of the device, technical and scientific information, and copies of proposed labeling. Section 814.37 provides requirements for an applicant who seeks to amend a pending PMA. Section 814.82 sets forth postapproval requirements FDA may propose, including periodic reporting on safety effectiveness, and reliability, and display in the labeling and advertising of certain warnings. Other potential postapproval requirements include the maintenance of records to trace patients and the organizing and indexing of records into

identifiable files to enable FDA to determine whether there is reasonable assurance of the device's continued safety and effectiveness. Section 814.84 specifies the contents of periodic reports.

**II. FDA Modernization Act of 1997**

The FDA Modernization Act of 1997 (FDAMA), enacted on November 21, 1997, to implement revisions to the act, streamlines the process of bringing safe and effective drugs, medical devices, and other therapies to the U.S. market. Several provisions of this act that affect the PMA process and impact collection of information have been or will be implemented by FDA and are discussed as follows.

Section 201(b) of FDAMA amends section 515(d) of the act to allow submission of data from investigations of earlier versions of a device, in support of a safety and effectiveness determination for a PMA. The data is valid if modifications to earlier versions of the investigational device, whether made during or after the investigation, do not constitute a significant change that would invalidate the relevance of the data. This section also allows for the submission of data or information relating to an approved device that are relevant to the design and intended use of a device for which an application is pending, provided the data are available for use under the act (i.e., available by right of reference or in the public domain).

Section 202 of FDAMA amends section 515(d) of the act to state that FDA will provide special review, which can include expedited processing of a PMA application, for certain devices intended to treat or diagnose life threatening or irreversibly debilitating diseases or conditions.

Section 205(a) of FDAMA amends section 513(a)(3) of the act (21 U.S.C. 360c(a)(3)) to allow sponsors planning to submit a PMA to submit a written request to FDA for a meeting to determine the type of information (valid scientific evidence) necessary to support the effectiveness of their device. FDA must meet with the requester and communicate in writing the agency's determination of the type of data that will be necessary to demonstrate effectiveness within 30 days after the meeting.

Section 205(c) of FDAMA amends section 515(d) of the act to state that PMA supplements are required for all changes that affect safety or effectiveness, unless such change involves modifications in a manufacturing procedure or method of manufacturing. Clearance for this information collection, included within a proposed rule, has already been sought by FDA in an earlier document (63 FR 20558, April 27, 1998).

Section 205(c) of FDAMA amends section 515(d) of the act to allow for approval of incremental changes in design affecting safety and effectiveness based on nonclinical data that demonstrate the change creates the intended additional capacity, function, or performance of the device; and clinical data included in the original PMA application or any supplement to that application that provides reasonable assurance of safety and effectiveness. If needed, FDA may require a sponsor to submit new clinical data to demonstrate safety and effectiveness.

Section 207 of FDAMA amends section 513 of the act to allow an applicant who submits a premarket notification submission (510(k)) and receives a not substantially equivalent (NSE) determination, placing the device into a class III category, to request FDA to classify the product into class I or II. The request must be in writing and sent within 30 days from the receipt of the NSE determination. Within 60 days from the date the written request is submitted to FDA, the agency must classify the device by written order.

If FDA classifies the device into class I or II, this device can be used as a predicate device for other 510(k)'s. However, if FDA determines that the device will remain in class III, the device cannot be distributed until the applicant has obtained an approved PMA or an approved investigational device exemption.

Section 208 of FDAMA amends section 513 of the act to allow PMA applicants to have the same access as FDA to data and information submitted by FDA to a classification panel, except data not available for public disclosure; the opportunity to submit information based on the PMA, through FDA, to the panel; and the same opportunity as FDA to participate in panel meetings.

Section 209(b) of FDAMA amends section 515(d) of the act to state that FDA must, upon the written request of the applicant, meet with that party within 100 days of receipt of the filed PMA application to discuss the review status of the application. With the concurrence of the applicant, a different schedule may be established. Prior to this meeting, FDA must inform the applicant in writing of any identified deficiencies and what information is required to correct those deficiencies. FDA must also promptly notify the applicant if FDA identifies additional deficiencies or of any additional information required to complete agency review.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

| 21 CFR Section | No. of Respondents | Annual Frequency per Response | Total Annual Responses | Hours per Response | Total Hours |
|---|---|---|---|---|---|
| 814.15, 814.20, and 814.37 | 52 | 1 | 52 | 837.28 | 43,539 |
| 814.82 | 37 | 1 | 37 | 134.68 | 4,983 |
| 814.84 | 37 | 1 | 37 | 10 | 370 |
| Total | | | | | 48,892 |

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

| 21 CFR Section | No. of Recordkeepers | Annual Frequency per Recordkeeping | Total Annual Records | Hours per Recordkeeper | Total Hours |
|---|---|---|---|---|---|
| 814.82(a)(5) and (a)(6) | 814 | 1 | 814 | 16.7 | 13,594 |
| Total | | | | | 13,594 |

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
Note: Statutory burden is not included on the burden chart.

## III. Reporting/Disclosure

The reporting burden can be broken out by certain sections of the PMA regulation: (1) § 814.15—Research conducted outside the United States, (2) § 814.20—Application, and (3) § 814.37—PMA amendments and resubmitted PMA's.

The bulk of the burden is due to the previous three requirements. Included in these three requirements are the conduct of laboratory and clinical trials as well as the analysis, review, and physical preparation of the PMA application. FDA's estimate of the hours per response (837.28) was derived through FDA's experience and consultation with industry and trade associations. Included in these three requirements are the conduct of laboratory and clinical trials as well as

the analysis, review, and physical preparation of the PMA application. FDA estimates, based on the 1985 study, that these requirements account for the bulk of the burden identified by manufacturers.

**IV. § 814.39—PMA Supplements**

Clearance for this information collection, included within a proposed rule, has already been sought by FDA in an earlier document (63 FR 20558).

**V. § 814.82—Postapproval Requirements**

Postapproval requirements concern approved PMA's for devices that were not reclassified and require an annual report. In the last decade (1988 to 1997), the range of PMA's which fit this category averaged approximately 37 per year (70 percent of the 52 annual submissions). Most approved PMA's have been subject to some restriction. Approximately half of the average submitted PMA's (26) require associated postapproval information (i.e., clinical trials or additional preclinical information) that is labor-intensive to compile and complete, and the other PMA's require minimal information. Based on its experience and on consultation with industry, FDA estimates that preparation of reports and information required by this section requires 4,983 hours (134.68 hours per respondent).

**VI. § 814.84—Reports**

Postapproval requirements described in § 814.82 require a periodic report. FDA has determined respondents meeting the criteria of § 814.84 will submit reports on an annual basis. As stated previously, the range of PMA's fitting this category averaged approximately 37 per year. These reports have minimal information requirements. FDA estimates that respondents will construct their report and meet their requirements in approximately 10 hours. This estimate is based on FDA's experience and on consultation with industry. FDA estimates that the periodic reporting required by this section will take 370 hours.

## VII. Recordkeeping

The recordkeeping burden in this section involves the maintenance of records to trace patients and the organization and indexing of records into identifiable files to ensure the device's continued safety and effectiveness. These requirements are to be performed only by those manufacturers who have an approved PMA and who had original clinical research in support of that PMA. For a typical year's submissions, 70 percent of the PMA's are eventually approved and close to 100 percent of those have original clinical trial data. Therefore, about 37 PMA's a year (52 annual submissions times 70 percent) would be subject to these requirements. Also, because the requirements apply to all active PMA's, all holders of active PMA applications must maintain these records. PMA's have been required since 1976, so there are around 814 active PMA's that could be subject to these requirements (22 years x 37 per year). Each study has approximately 200 subjects, and, at an average of 5 minutes per subject, there is a total burden per study of 1,000 minutes, or 16.7 hours. The aggregate burden for all 814 holders of approved original PMA's, therefore, is 13,594 hours.

The applicant determines which records should be maintained during product development to document and/or substantiate the device's safety and effectiveness. Records required by the current good manufacturing practice/quality systems regulation (21 CFR part 820) may be relevant to a PMA review and may be submitted as part of an application. In individual instances, records may be required as conditions to approval to ensure the device's continuing safety and effectiveness.

Respondents to this information collection are persons filing an application with the Secretary of Health and Human Services for approval of a class III medical device. Part 814 defines a person as any individual, partnership, corporation, association, scientific or academic establishment,

government agency or organizational unit, or other legal entity. These respondents include manufacturers of commercial medical devices in distribution prior to May 28, 1976 (the enactment date of the Medical Device Amendments).

Dated: January 20, 1999

William Hubbard

William K. Hubbard
Associate Commissioner for Policy Coordination

[FR Doc. 99–???? Filed ??–??–99; 8:45 am]

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